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FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
TUCKER, ZACHARY C	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/622,055	CERNERUD ET AL.	
	Examiner	Art Unit	
	Zachary C. Tucker	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-44* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☒ Claim(s) *1-14,16,19,28-33 and 38* is/are allowed.

6)☒ Claim(s) *17,18,24,25,27,34-37 and 39-44* is/are rejected.

7)☒ Claim(s) *21-23 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *30Jun06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

As requested by applicants in the correspondence filed 30 June 2006 (hereinafter "present amendment"), which is in reply to the Office action mailed 28 December 2005 (hereinafter "previous Office action"), claims 1, 13 and 16-19 have been amended, claim 15 has been cancelled and new claims 29-44 have been added. The title of the application has also been amended as requested, to now read "Amino-Substituted 1*H*-pyrazin-2-ones and 1*H*-quinoxaline-2-ones."

Election/Restrictions

The present amendment overcomes the rejections set forth in the previous Office action, placing the subject matter of elected Group I in condition for allowance. Thus, the conditions necessary for rejoinder of Groups II and IV subject matters have been met. Group II, claims 14 and 16-19, and Group IV, claims 21-27 are hereby rejoined and the Requirement for Restriction between the compounds according to Group I, pharmaceutical compositions and methods of treatment according to Group II and methods for preparing Group I compounds according to Group IV is hereby WITHDRAWN. Group III subject matter, claim 20, is deemed not to be commensurate in scope, and is therefore not rejoined.

Claim 15, which was part of Group II, has been cancelled by virtue of the present amendment, and new claims 29-44 are part of Group II as they are drawn to methods for treating various medical conditions.

Status of Claim Rejections - 35 USC § 112

In the previous Office action, claims 1-13 and 28 were rejected under 35 U.S.C. 112, first and second paragraphs, because the claimed prodrug forms of the

compounds according to those claims were found not to be enabled by the accompanying disclosure and also because the term "prodrug forms" rendered said claims indefinite in scope. Claim 13 was found to be further indefinite because of a lack of antecedent basis of the "solvates" recited therein, in claim 1 from which claim 13 depends.

In view of the present amendment, which strikes all "prodrug" language from the instant claims, the rejections under the first and second paragraphs of 35 U.S.C. 112, is hereby withdrawn. The lack of antecedent basis problem with claim 13 has also been corrected by the present amendment.

Title of the Application

Objection to the disclosure was set forth in the previous Office action because the title was deemed not to be descriptive of the disclosed and claimed subject matter. In view of the present amendment to the title of the application, the objection to the disclosure is hereby withdrawn.

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New Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following new rejections under 35 U.S.C. 112 are seen as necessary in view of the rejoinder of previously withdrawn claims.

Claims 17, 18, 34-38 and 39-44 are rejected under 35 U.S.C. 112, first and second paragraphs, as failing to comply with the enablement requirement and also for being of indefinite scope. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or

with which it is most nearly connected, to make and/or use the invention, or to understand the scope of the method/process applicants possess the right to exclude others from practicing, should the indicated claims be patented.

Treatment of Alzheimer's disease, "a disorder or medical condition that is associated with neuroleptic drug therapy," memory disorders, mood disorders, sleep disorders, sexual function disorders, fibromyalgia, thrombotic illness, autism, Parkinson's disease and "diabetic complications" as specified in claims 17, 18, 34-38 and 39-44, is not enabled by the disclosure. Additionally, the terms "a disorder or medical condition that is associated with neuroleptic drug therapy" and "diabetic complications" are not clear and well-defined such that the scope of a claim in which said terms are recited (claims 18 and 44, respectively, that is) is not distinctly pointed out and claimed.

Remarks by applicants' counsel, which accompany the present amendment, include citation of several references from various medical and scientific journals, which are offered in support of applicants' contention that all methods according to the instant claims are indeed enabled by the disclosure. Compounds according to the instant claims are $5HT_{2A}$ receptor antagonists (specification, page 70), and the references cited by applicants report and discuss some pharmacological effects of drugs having this activity.

In the previous Office action, at pages 10-13, the examiner included preliminary comments as to degree to which the then-withdrawn method-of-use claims were enabled. Instant claim 16 has been amended to coincide with the subject matter indicated by the examiner as being enabled by the disclosure, and is allowed.

Although instant claim 16 is allowed, methods according to instant claims 17, 18, 34-38 and 39-44 are not, as the methods recited therein are not enabled by the disclosure.

In making the determination of whether or not a claimed invention is enabled by the accompanying disclosure, the Office relies on factors promulgated in the decision rendered in *In re Wands*, the so-called "Wands factors," which are:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, 858 F.2d 731,737 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

Each will be addressed in the following.

(A) The claims at issue are drawn to methods of treating Alzheimer's disease, "a disorder or medical condition that is associated with neuroleptic drug therapy," memory disorders, mood disorders, sleep disorders, sexual function disorders, fibromyalgia, thrombotic illness, autism, Parkinson's disease and "diabetic complications."

Alzheimer's disease, autism and Parkinson's disease are fairly narrow in scope, as they deal with discrete, known and understood disease processes. "A disorder or medical condition that is associated with neuroleptic drug therapy," memory disorders, mood disorders, sleep disorders, sexual function disorders, fibromyalgia, thrombotic illness and "diabetic complications," on the other hand, are extremely broad in scope and in the case of "diabetic complications" and "a disorder or medical condition that is associated with neuroleptic drug therapy" are additionally of indeterminate scope.

"Mood disorders" includes any psychiatric disorder affecting the mood, arguably any and all psychiatric disorders. "Memory disorders" includes *any* disorder affecting memory, such as senility, Alzheimer's disease, residual effects of head trauma, fetal alcohol syndrome, amnesia (caused by an injury or a chemical insult) and others. "Sleep disorders" refers to any and all sleep disturbances, including insomnia, narcolepsy, somnambulism, nocturnal enuresis and hypersomnia, to name a few. "Sexual function disorders" includes premature ejaculation, anorgasmia, hypoactive sexual desire disorder, sexual aversion disorder, erectile dysfunction and dyspareunia, to name a few. "Thrombotic illness including stroke" includes stroke, of course, but also includes *any* disorder having *anything* to do with blood clotting. Hemophilia, which is a genetic disease that causes a severe deficiency in blood clotting factors, is included in the term "thrombotic disorder," as well as, intermittent claudication, transient ischemic attacks, myocardial infarction, pulmonary embolism (if caused by thromboembolic event), and *any* thromboembolism. Thrombocytopenia, which is often secondary to alcoholism, is also included within the scope of "thrombotic disorder." Fibromyalgia is a condition that is marked by widespread pain, but includes so many different signs and symptoms, including memory problems and depression, that treatment of fibromyalgia in general requires treatment of a panoply of different symptoms, not to mention the fact that its diagnosis is often contentious and many experts remain doubtful about the existence of the condition. "Diabetic complications" does not denote any particular group of conditions or symptoms, but includes rather *any* complication experienced by any person afflicted with diabetes. It is impossible to determine whether or not the "complications" are actually secondary to the diabetes itself or if they are primary

symptoms which are part of the disease itself. For example, is diabetic retinopathy part of the course of the disease diabetes or is it a "complication" of diabetes? Is polyuria a "complication" of diabetes or is it actually part of the disease process itself? Lastly, the term "a disorder or medical condition that is associated with neuroleptic drug therapy" refers to *any* disorder or medical condition which occurs in *any* individual taking *any* neuroleptic drug. This term could include any number of medical conditions either caused by or merely *associated* with the same individual who is taking a neuroleptic drug. For example, if an individual taking an antipsychotic drug happens to also be afflicted with a cancer, then instant claim 18 would cover the treatment of whichever cancer that was. If the individual taking the antipsychotic drug happens to have ingrown toenails, then instant claim 18 would cover the treatment of ingrown toenails. The disorder or medical condition associated with neuroleptic drug therapy need not have anything to do with neuroleptic drug therapy or the indication for which the neuroleptic drug is administered to the individual.

(B) The indicated claims are drawn to medical treatment methods.

(C) As indicative of the state of the art with respect to the treatment of the conditions/diseases allegedly treated by the methods specified in the above-captioned claims, the examiner would rely on the evidence presented by applicants' counsel in the correspondence filed 30 June 2006. It would seem that applicants' counsel has put forth what he believes to be the best possible argument, and indeed it is persuasive in part, insofar as those conditions for which the examiner has relented his previously held position (treatment of urinary incontinence, pain, glaucoma and depressive disorders

including depression with coexisting diabetes is now seen as being enabled by the disclosure).

Evidence presented by applicants' counsel is directed to showing that treatment of glaucoma, urinary incontinence, depression with co-existing diabetes, memory disorders, sleep disorders, diabetic complications, sexual dysfunction, fibromyalgia, neuroleptic drug therapy, thrombotic illness, pain, and stroke is enabled by the disclosure of the $5HT_{2A}$ receptor antagonists according to the present invention. Treatment of glaucoma, urinary incontinence, depression with co-existing diabetes and pain have been found to be enabled by the disclosure.

So, the evidence presented by applicants' counsel insofar as treatment of memory disorders, sleep disorders, diabetic complications, sexual dysfunction, fibromyalgia, neuroleptic drug therapy, thrombotic illness and stroke will be focused upon here.

Thrombotic illness:

Applicants' argument states that studies in animal models have shown that $5HT_{2A}$ receptor antagonists can be effective in the treatment of thrombotic diseases. What is addressed, however, is only those diseases which involve *too much* clotting activity, like chronic arterial occlusive disease. Drugs with $5HT_{2A}$ receptor antagonist activity would only worsen a disease in which too little thrombotic activity was the problem, such as hemophilia or thrombocytopenia.

So, the argument is not persuasive because the full scope of "thrombotic illness" includes diseases both in which too much and too little clotting activity is the problem.

Stroke:

Treatment of stroke is enabled by the disclosure, according to applicants, because "several antagonists of 5-HT2 are in various stage [*sic*] of experimental or clinical trials for the treatment of stroke and some positive results have been observed with 5-HT2 antagonists." No evidence is offered to back up this assertion, neither is the exact nature of the "some positive results" characterized. An article is cited, however, authored by Dietrich et al (*J. Cerebral Blood Flow and Metab.*, vol. 9, pages 812-820, 1989) and is included in the Information Disclosure Statement filed 30 June 2006. Dietrich et al concludes that the $5HT_{2A}$ receptor antagonist ketanserin might prove useful in stroke management. Only in a strictly-controlled experimental model of stroke in rats was this positive effect of ketanserin observed. The authors only studied the effect of ketanserin administered *before* the simulated cerebral infarct, not after, as would necessarily be the case in a real-world application of the method according to instant claims 40 and 41. Thus, the results reported by Dietrich et al only amount to a showing that there is some role that 5HT plays in the pathogenesis of stroke. At page 818, in the paragraph bridging the first and second columns, Dietrich et al acknowledge that ketanserin has some norepinephrine antagonizing activity in addition to its 5HT antagonist activity, and that this additional effect that the drug has could have influenced the results reported in that article. Compounds according to the instant invention possess no such activity, so ketanserin is not completely equivalent to the inventive compounds. For these reasons, the evidence provided by applicants is not probative in showing that treatment of stroke is enabled by the instant specification.

The subject of the rejection under 35 U.S.C. 112, first paragraph at hand, however, is that treatment of the conditions stated in the opening paragraph of this section is *not* enabled by the instant specification, specifically by the disclosure of the compounds of the present invention, which are $5HT_{2A}$ receptor antagonists.

Neuroleptic Drug Therapy:

Only neuroleptic-induced extrapyramidal symptoms are addressed as the "a disorder or medical condition that is associated with neuroleptic drug therapy" in the section devoted to showing that the method according to instant claim 18 is enabled by the instant specification. It is readily apparent that extrapyramidal symptoms are but one out of thousands upon thousands of possible disorders or medical conditions merely "associated with neuroleptic drug therapy," so it is self-evident that regardless of whether or not a $5HT_{2A}$ receptor antagonist is effective for treating extrapyramidal symptoms induced by neuroleptic drug therapy, the full scope of instant claim 18 is nowhere close to being enabled by the disclosure. A claim drawn to the treatment of neuroleptic drug-induced extrapyramidal symptoms was indicated as being enabled by the disclosure in the interview summary included with the previous Office action.

Fibromyalgia:

The section of applicants' argument wherein treatment of fibromyalgia is alleged to be enabled by the disclosure of the $5HT_{2A}$ receptor antagonist compounds according to the present invention refers to a study authored by Stratz et al, from *Zeitschrift für Rheumatologie*, vol. 50, pages 21-22 (1991), in which ketanserin, the $5HT_{2A}$ receptor antagonist discussed in the preceding section headed "Stroke," was found to decrease

pain and tender points, decrease anxiety and increase quality of sleep in fibromyalgia patients. These results are seen as nothing more than a showing that a $5HT_{2A}$ receptor antagonist is effective for treatment of pain, anxiety and sleeplessness, which is well-known and accepted by the medical community. Treatment of the complicated and not well-understood symptomatology and etiology of fibromyalgia is not shown to be enabled by the results reported by Stratz et al, rather the report demonstrates that ketanserin has the expected therapeutic benefits (improvement in pain status, anxiety, and sleep) in fibromyalgia patients as well as in other persons. Treatment of pain and anxiety are enabled by the instant specification.

Sexual Dysfunction:

Only a brief statement to the effect of: "Sexual dysfunction often occurs in patients treated with selective serotonin reuptake inhibitors (SSRI). 5-HT_{2A} antagonists have been shown to reverse SSRI-induced dysfunction." appears in the section of applicants' remarks devoted to showing that treatment of sexual dysfunctions is enabled by the disclosure. While this may be true, the type of sexual dysfunction caused by SSRI drugs is very limited – ejaculatory delay in males and decreased sexual desire in both sexes. Thus, the therapeutic efficacy of a $5HT_{2A}$ receptor antagonist drug, such as those according to the present invention, in treating sexual dysfunction would be similarly limited. The full scope of "sexual dysfunction" includes many conditions not even remotely associated with 5HT, like sexual aversion disorder or the opposite – nymphomania in females and its equivalent in males, satyriasis. To rely on the reasoning put forth by applicants, premature ejaculation, which is one sexual dysfunction that can be successfully treated with SSRI drugs, would be expected to be

worsened by a drug having the opposite activity, like the $5HT_{2A}$ receptor antagonists according to the present invention. The full scope of "sexual dysfunction" cannot be successfully treated with compounds according to the present invention.

Diabetic Complications:

Diabetic complications are myriad, yet only two are discussed in the section of applicants' remarks devoted to showing that treatment of diabetic complications in general is enabled by the disclosure of the $5HT_{2A}$ receptor antagonist compounds according to the present invention. So, even if applicants' remarks are accurate and true, the full scope of "diabetic complications" cannot possibly be treated with $5HT_{2A}$ receptor antagonist compounds. Diabetic retinopathy and nephropathy are by no means representative of the full scope of all diabetic complications. Neuropathy is one of the most significant and debilitating of all diabetic complications, yet is not even mentioned in applicants' remarks.

Sleep Disorders:

In the section of applicants' remarks devoted to showing that treatment of sleep disorders, in general, is enabled by the instant specification, only insomnia and obstructive sleep apnea are addressed. Even if the treatment of these two conditions is enabled fully by the disclosure, the full scope of "sleep disorders" is not approached in the least. Somnambulism (sleep walking), nocturnal enuresis (bed-wetting), narcolepsy, restless leg syndrome, jet lag and shift work sleep disorder, to name a few are some other relatively common sleep disorders, and are not even mentioned in the instant specification, much less in applicants' remarks. If compounds according to the present invention are effective for treating insomnia and sleep apnea, then a disorder such as

narcolepsy, in which sudden and profound attacks of sleepiness are the primary symptom, would be expected to be worsened by drugs having the activity possessed by compounds of the present invention. Treatment of the full scope of "sleep disorders" is not enabled by the instant specification.

Autism:

At the outset, the examiner would point out that autism is not treatable with any pharmacological intervention. Only some of the symptoms of this pervasive inherited condition are treatable with drugs. The patent mentioned in the brief section of applicants' remarks devoted to showing that treatment of autism is enabled by the instant specification shows that a $5HT_{2A}$ receptor antagonist attenuates hyperactivity induced by the glutamate (NMDA receptor) antagonist MK-801, which allegedly is evidence that a $5HT_{2A}$ receptor antagonist is an effective treatment strategy for autism.

The "hypoglutamatergic model of autism" (induced by the drug MK-801) addresses only some of the cognitive symptoms of autism, not the entire clinical picture. Therefore, a treatment that attenuates some aspect of the cognitive symptoms of autism is does not constitute a treatment for autism *per se*, rather it is only a treatment for some of the symptoms. As evidenced by the following reference, which is submitted with this Office action:

> Nilsson et al, "A behavioural pattern analysis of hypoglutamatergic mice – effects of four different antipsychotic agents" *Journal of Neural Transmission*, vol. 108, pages 1181-1196 (2001).

MK-801 treatment in rodents only reproduces the meager behavioral repertoire typical of autistic persons. The full scope of autistic symptoms cannot be reproduced in rodents, such as the impaired verbal communication and restricted imagination (page 1194). Consequently, an assertion that some drug which serves to attenuate behavioral

effects of MK-801 in a rodent would constitute a "treatment" for autism cannot be substantiated, simply because the entire clinical picture of the disease cannot be observed in the rodent.

Memory Disorders:

Applicants' comments which purport to show that treatment of "memory disorders," in general, is enabled by the disclosure of the $5HT_{2A}$ receptor antagonists according to the present invention only pertain to cognitive function impairment seen in schizophrenia, and scopolamine-induced hyperlocomotion in rats. These two phenomena in no way come close to the full scope of what is actually embraced by "treatment of memory disorders." Successful treatment of cognitive dysfunction in schizophrenic patients, by administering a $5HT_{2A}$ receptor antagonist does not necessitate that all memory disorders are similarly treatable. Applicants' statement that "Scopolamine-induced hyperlocomotion in the rat has sometimes been used as a model of behavioral disturbances related to cholinergic deficiency states such as Alzheimer's disease" only obliquely invokes Alzheimer's disease, and says nothing about *memory* disturbances related to Alzheimer's. No statement to the effect of "a $5HT_{2A}$ receptor antagonist will treat Alzheimer's disease" is made, nor would such a statement actually be true.

(D) The level of ordinary skill with respect to the methods according to instant claims 17, 18, 34-38 and 39-44 is that of a physician experienced in the practice of whichever medical discipline is most relevant to the condition being treated.

(E) Medicine is sometimes predictable, sometimes not. With respect to the methods according to instant claims 17, 18, 34-38 and 39-44, it can positively be predicted that

the full scope of none of Alzheimer's disease, "a disorder or medical condition that is associated with neuroleptic drug therapy," memory disorders, mood disorders, sleep disorders, sexual function disorders, fibromyalgia, thrombotic illness, autism, Parkinson's disease or "diabetic complications" could be treated by administering a compound of the present invention to an individual afflicted therewith.

(F) The inventor has provided little guidance for practicing the methods according to instant claims 17, 18, 34-38 and 39-44. Only these two paragraphs of the specification actually speak to the real practice of the methods of treatment:

> The typical dose of the active substance varies within a wide range and will depend on various factors such as, for example, the individual requirement of each patient and the route of administration. In general, oral and parenteral dosages will be in the range of 5 to 1000 mg per day of active substance, preferably 50 to 150 mg per day.
>
> The dose level, frequency of dosage, mode of administration, of the specific compound will vary depending on a variety of factors including the potency of the specific compound employed, the metabolic stability and length of action of that compound, the patient's age, body weight, general health, sex, diet, mode and time of administration, rate of excretion, drug combination, the severity of the condition to be treated, and the patient undergoing therapy.

As is readily apparent, there is no teaching specific to any particular disease state, no dosage range more specific than "50 to 150mg per day" and no guidance at all as to how long the duration of treatment should be.

(G) There are no working examples of the methods according to claims 17, 18, 34-38 and 39-44.

(H) No amount of experimentation would enable the physician of ordinary skill to practice the methods according to claims 17, 18, 34-38 and 39-44. To do so would not

medically be possible, because there are so many disparate types of conditions within the scope of these claims that a compound having but one pharmacological activity, namely antagonism at the $5HT_{2A}$ receptor, could not address all of the different etiologies thereof. For example, those diseases caused by *too little* activity at the $5HT_{2A}$ receptor would most likely be worsened by compounds of the present invention.

Claims 18 and 44, in addition to not being enabled by the disclosure, are indefinite under the second paragraph of 35 U.S.C. 112, because the metes and bounds of "a disorder or medical condition associated with neuroleptic drug therapy" is not specific to any disorder or medical condition, and "diabetic complications" does not differentiate between those secondary effects of diabetes (like limb amputation) and those phenomena directly associated with the diabetes disease process itself (like hyperglycemia).

Claims 24, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the last line of claim 25, the phrase "at an elevated temperature" is recited as a limitation. "Elevated temperature" is a relative term, akin to "high temperature" or "while hot." The specification does not provide a standard for ascertaining the requisite degree of elevated temperature, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Since applicants are specifying the process of claim 25, wherein the last step is conducted only at elevated temperature, the public, to

understand exactly what is covered by the claim, should it be patented, must understand what temperatures applicants consider to be "elevated" and what applicants consider not to be so. A process according to instant claim 25 wherein the final step is not conducted at an elevated temperature would not be covered by the claim, yet there is no means of determining which temperatures would qualify as such.

The examiner recommends striking "at an elevated temperature" from claim 25.

Claim Objections

Claims 21-23 and 26, although rejoined as indicated hereinabove, are objected to for being illegible. In claim 21, from which all of 22, 23 and 26 depend and therefore incorporate limitations of, the structure of the formula (II) intermediate compound is includes a "$(CH_2)_n$" superimposed over an "X." Exactly where on the diagram the "$(CH_2)_n$" is supposed to be is not clear from the claim; it is floating by itself, not connected to the rest of the structure. Since it would be overly speculative on the part of the examiner to presume he knows what applicants intended by this structure diagram, claims 21-23 and 26 are objected to and have not been further addressed on the merits in this Office action. Upon correction so as to render formula (II) in claim 21 legible, claims 21-23 and 26 will be examined and most likely allowed, as there do not appear to be any deficiencies in the language of those claims, only in the structure diagram (II).

Allowable Subject Matter

Claims 1-14,16,19,28-33 and 38 are allowed.

Reasons for indicating the allowability of the compounds were provided in the previous Office action, at page 10.

Claims 24, 25 and 27 would be allowable if the rejection under 35 U.S.C. 112, second paragraph, were overcome. The examiner recommends striking the phrase "at an elevated temperature" from the last line of the claim.

Method of treatment claims 16, 29-33 and 38 are allowed in view of the reference authored by de Angelis et al, cited in the previous Office action, page 11, the references cited by applicants in the remarks accompanying the present amendment and the accompanying arguments.

Comment

Although its presence in the remarks accompanying the present amendment is no more than a red herring, as the term "prophylaxis" has been struck from the claims, the examiner would address the contention put forth by applicants' counsel that "prophylaxis" does not necessitate complete elimination of the disease or condition. It seems that applicants' counsel is stating (page 21 of the correspondence filed 30 June 2006) that because "other benchmarks" in addition to the broad interpretation of the term "prophylaxis" advocated by the Office (that prophylaxis necessarily embraces prevention) are encompassed the term, then the broad interpretation is somehow not embraced by the term. To say the least, this position presents logical problems.

To make the record clear, and to show that the examiner was not reading the term "prophylaxis" in a manner inconsistent with its commonly accepted meaning, the definition of the word from Webster's II New Riverside University Dictionary © 1994

Houghton Mlfflin Company is submitted with this Office action. According to Webster's, "prophylaxis" means "protective treatment for or prevention of disease."

Conclusion

Applicant's amendment necessitated the new grounds of rejection presented in this Office action (newly added claims, and amendment to claims of elected Group I which amendment necessitated rejoinder and rejection of previously withdrawn claims). Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached Monday to Friday from 5:45am to 2:15pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

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